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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
ROONEY, NORA MAUREEN	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,927	FIEBIG ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15,16,20-23 and 25-34* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 15, 20-23, 25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on 06/03/2008 is acknowledged.

2. Claims 1-13, 15-16, 20-23 and 25-34 are pending.

3. Claims 1-12 and 16 and stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/29/2007.

4. Claims 13, 15, 20-23 and 25-34 are currently under examination as they read on a polypeptide encoded by the nucleic acid sequence of SEQ ID NO:1 and a pharmaceutical composition or vaccine thereof.

Claim Objections

5. Claims 13 and 33-34 are objected to because of the following informalities:

In claim 13, line 8, the word "or" should be deleted;

In claim 13, line 10, there should be a comma after SEQ ID NO:6;

In claim 13, line 16-17, there should be a "or" after SEQ ID NO:6 and the comma should be deleted;

In claim 33, line 2, there should be an 'a" before the term 'single nucleotide polymorph';

In claim 33, line 3, there should be an 'or' after 'SEQ ID NO;1,';

In claim 33, line 4, there should be a period and not a comma at the end of the claim;

In claim 34, line 2, there should be an "in" or an alternate word or phrase between the words "forth" and "clones";

In claim 34, lines 4, 8 and 9, the terms '5235', '1264' and '5384' should be changed to reflect actual amino acid variations set forth in the specification. The Examiner believes they should be S235, I264 and S384; and

In claim 34, the claim must be a single sentence that include the recitations of clones 1-11 in the phrasing and punctuation.

Appropriate correction is required.

6. Applicant is advised that should claim 20 be found allowable, claim 25 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

7. The following rejections are necessitated by the amendment filed on 06/03/2008.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 22 stands rejected and claims 28 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 recites "fragment 1-200", "amino acids 1-200 of the polypeptide of claim 13", "fragment 185-500"; and "amino acids 185-500 of the polypeptide of claim 13" without reference to a specified sequence identification number making the claim indefinite. The recitation of positions within the polypeptide is indefinite without a reference sequence to which it refers. It is noted that claim 22 encompasses a broad genus of polypeptides and variants that would not have the same position numbering as SEQ ID NOs 2, 4 and 6.

Applicant's argument filed on 06/03/2008 has been fully considered, but is not found persuasive.

Applicant argues:

> "The rejection, not specifically discussed herein, is moot in view of the amendments. Withdrawal of the rejection is respectfully requested."

It is the Examiner's position that Applicant's amendments do not overcome the instant rejections. Therefore, the rejection stands for reasons of record and set forth *supra*.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 13, 15 and 20-23 stand rejected and claims 25-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: polypeptides of SEQ ID NO: 2, 4, 6 encoded by SEQ ID NO:1, 3 or 5, respectively, the variants of SEQ ID NO:2 in clones 1-11 and a composition thereof, does not reasonably provide enablement for: A polypeptide which is (a) a polypeptide which comprises the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6, (b) a polypeptide comprising a polypeptide sequence which is encoded by a the polynucleotide sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5, or (c) **a variant polypeptide which comprises at least 90.8% sequence identity** to the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 (d) **a polypeptide which comprises at least 79.9% sequence identity to the polypeptide comprising amino acids 219 to 362** of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6, (e) **a polypeptide which comprises at least 69.7% sequence identity to the polypeptide comprising amino acids 219 to 251** of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 of claim 13; A **pharmaceutical composition** comprising at least one polypeptide according to Claim 13 and a pharmaceutically acceptable carrier of claim 15; an **immunotherapeutic vaccine** comprising a

polypeptide of claim 13 and an acceptable carrier, wherein said **vaccine** is capable of generating an immunomodulatory, T-cell response in a host of claim 20; an immunomodulatory, T-cell-reactive polypeptide fragment **which comprises a partial sequence of 50 to 350 amino acids of at least one polypeptide of claim 13** of claim 21; an immunomodulatory, T-cell-reactive polypeptide fragment which comprises (a) **fragment 1-200, with amino acids 1-200 of the polypeptide of claim 13**, or (b) **fragment 185-500, with amino acids 185-500 of the polypeptide of claim 13** of claim 22; **the variant polypeptide according to Claim 13** (c) which comprises a mutation, wherein said mutation results in the replacement of at least one cysteine residue of a polypeptide whose sequence is set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6 with another amino acid residue of claim 23; **an immunotherapeutic vaccine** comprising a **polypeptide of claim 13** and an acceptable carrier, wherein said **vaccine** is capable of generating an immunomodulatory, T-cell response in a host of claim 25; **A polypeptide according to claim 13** wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cell reactive response in a host of claim 26; an **immunotherapeutic vaccine** comprising **a polypeptide of claim 21** and an acceptable carrier, wherein said **vaccine** is capable of generating an immunomodulatory, T-cell response in a host of claim 27; an **immunotherapeutic vaccine** comprising **a polypeptide of claim 22** and an acceptable carrier, wherein said **vaccine** is capable of generating an immunomodulatory, T-cell response in a host of claim 28; An **immunotherapeutic vaccine** comprising **a polypeptide of claim 23** and an acceptable carrier, wherein said **vaccine** is capable of generating an immunomodulatory, T-cell response in a host of claim 29; A **pharmaceutical composition** comprising **at least one polypeptide according to claim 21** and a pharmaceutically acceptable

carrier of claim 30; A **pharmaceutical composition** comprising **at least one polypeptide according to claim 22** and a pharmaceutically acceptable carrier of claim 31; A **pharmaceutical composition** comprising at **least one polypeptide according to claim 23** and a pharmaceutically acceptable carrier of claim 32; **A** polypeptide which comprises **(a) a polypeptide which is encoded by single nucleotide polymorph of a polynucleotide whose sequence is set forth in SEQ ID NO: 1, (b) a single amino acid polymorph of a polypeptide whose sequence is set forth in SEQ ID NO: 2** of claim 33; A polypeptide which comprises **a polypeptide variant of the sequence set forth in SEQ ID NO: 2 with** the amino acid variations set forth clones 1 to 11: (a) clone 1: L54, I57, V62, S76, T100, N107, Y137, P141, T142, K189, Q219, K221, L227, I231, 5235, T237, V238, K248, A258, I264, K270, K282, L287, P299, A321, L322, S332, Q346, P347, T351, L357, N358, V362, S384, A410, D419, Y456, A457, K460, E472; (b) clone 2: L54, I57, V62, T76, T100, N107, Y137, P141, T142, K189, Q219, K221, I231, S235, T237, V238, K248, A258, 1264, K270, K282, L287, P299, A321, L322, S332, Q346, P347, T351, L357, N358, V362, 5384, A410, D419, Y456, A457, K460, E472; (c) clone 3: P141, K282, L287, P299, L347, E351; (d) clone 4: G289, A410, D419, Y456, A457, K460, E472; (e) clone 5: L347, E351, S384, A410, D419, Y456, A457, K460, E472; (f) clone 6: NI07, Y137, P141, T142, K189, Q219, K221, I231, S235, T237, V238, K248, A258, I264, K270, K282, L287, P299, A321, L322, 5332, Q346, P347, T351, L357, N358, V362, S384, A410, D419, Y456, A457, K460; (g) clone 7: K248, A258, I264, K270, K282, L287, P299, A321, L322, S332, Q346, P347, T351, L357, N358, V362, S384; (h) clone 8: Q219, K221, I231, S235, T237, V238, K248, A258, I264, K270, K282, L287, P299, E351; (i) clone 9: M231, T246, A251, C263, G289, L307, L309, E334; (j) clone 10: Q219, K221, I231, S235, T237,

M238, V242, V246, K248, A258, I264, K270, K282, L287, P299, A321, L322, S332, Q346, P347, T351, N358, V362, S384, insertion of GA between positions 407 and 408, N452, Y456, A457, K460, E472; and (k) clone 11: insertion of GA between positions 407 and 408 of claim 34. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses only the nucleic acid sequences SEQ ID NO:1, 3 and 5 encoding the polypeptides of SEQ ID NO:2, 4 and 6, respectively and the variants of SEQ ID NO:2 in clones 1-11.

There is insufficient guidance in the specification as filed as to how the skilled artisan would make and use the various polypeptides recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for the claimed functions. Without detailed direction as to which amino acids are essential to the function of the encoded polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of protein and peptide sequences encompassed by the instant claims would exhibit the claimed functional characteristics, of being immunogenic and induces an immunomodulatory T-cell reactive response in the host other than

the polypeptides of SEQ ID NO:2, 4 and 6 encoded by the nucleic acids of SEQ ID NO:1, 3 and 5 and the variants of SEQ ID NO:2 in clones 1-11.

The art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. teaches that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (PTO-892 mailed on 12/03/2007, Reference U; in particular, Table 2). Bowie et al. teaches that determination of three-dimensional structure from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (PTO-892 mailed on 12/03/2007, Reference V; page 1306 in particular). Thus, it is highly unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In view of this unpredictability; the skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity *over the full length of SEQ ID NO:2, 4 or 6* of the variants of SEQ ID NO: 2 in clones 1-11 to *share the same function* as the polypeptide of SEQ ID NO:2, 4 or 6 and the variants of SEQ ID NO: 2 in clones 1-11. The limitations of

"immunotherapeutic vaccine" in claims 20, 25, 27-29, "capable of generating an immunomodulatory, T-cell response in a host" of claims 20, 25 and 27-29; "wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cells reactive response in a host" in claim 26; and "immunomodulatory, T-cell reactive polypeptide fragment" in claims 21-22 are not seen as providing a requisite functional activity since numerous functional activities are encompassed by the specification and claims. The specification does not provide sufficient guidance as to which amino acids may be substituted, deleted, inserted and/or added and still retain the requisite function.

There is insufficient guidance in the specification regarding which partial sequences or combination of partial sequences of SEQ ID NO:2, 4, 6 and variants of SEQ ID NO:2 in clones 1-11 that are immunomodulatory and T cell-reactive. The term immunomodulatory implies that the immune system is changed, but no specific changes are recited. Therefore, the term 'immunomodulatory' encompasses just about any reaction by any cells or pathways related to the immune system. In the same way, the term 'T-cell reactive' is largely undefined. Any fragment or processed subsequence of the fragment that induces any T cell response or interaction is encompassed by the instant claims.

The specification does not provide support for any polypeptide "comprising" fragments of SEQ ID NO:2, 4, 6 or the variants of SEQ ID NO:2 in clones 1-11 "with" the recited variations. The terms 'comprising 'and 'with' are open language. As written, the claim encompasses an enormous number of undisclosed polypeptides and peptides that may include

sequence that is unrelated to the polypeptides of SEQ ID NO:2, 4 or 6 encoded by SEQ ID NO:1, 3, 5 or the variants of SEQ ID NO:2 in clones 1-11 that could independently posses the requisite function.

Also at issue is whether or not the claimed composition would function as 'pharmaceutical composition' and/or 'vaccine.' In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition or vaccine as claimed, absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical compositions or vaccine are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

Further, a vaccine is a composition to induce specific immunity that **prevents** or protects against a specific disease caused by a specific agent. The first criterion in judging a vaccine is the level of antibody (humoral immune response) before and after immunization. The success of the vaccination is judged by the extent of increase in the level of antigen - specific antibody. The second criterion for a vaccine is its ability to stimulate memory T lymphocytes (cell-mediated immune response) (See Immunology, Kuby, Fourth Edition, Chapter 18 in particular, PTO-892 mailed on 12/03/2007; Reference W). The specification provides no information on the vaccine formulation comprising any polypeptide, derivative or fragment of SEQ ID NO:2, 4 or 6 or the variants of SEQ ID NO:2 in clones 1-11 which is able to exhibit antigen-specific antibody

response, stimulated memory T lymphocytes and to protect or prevent against allergy. Vaccines by definition trigger an immunoprotective response in the host vaccinated and a mere antigenic response is insufficient. Further at issue is whether or not the claimed intended use would function to "prevent" allergy. The specification provides no in vivo data to support the claimed subject matter. The specification fails to provide guidance as to how to totally prevent (100% prevention) allergy using a vaccine or pharmaceutical composition comprising any polypeptide, derivative or fragment of SEQ ID NO:2, 4 or 6 or the variants of SEQ ID NO:2 in clones 1-11. The invention may reduce the likelihood of an allergy by administering the compound of SEQ ID NO:2, 4 or 6 or the variants of SEQ ID NO:2 in clones 1-11, but the specification does not disclose how to totally prevent allergy. Therefore, the specification does not provide sufficient guidance on how to sufficiently prevent the occurrence of allergy by administering the claimed compound.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited nucleic acid sequences and still encode a polypeptide that maintains the functional properties of the polypeptide of SEQ ID NO:2, 4, 6 or the variants of SEQ ID NO:2 in clones 1-11 is unpredictable, as is the identity of which subsequences would encode a functional polypeptide; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicant's arguments filed on 06/03/2008 have been fully considered, but are not found persuasive.

Applicant argues:

"..Applicants' specification discloses a vast number of polypeptide species which comprise the claimed activity. See, Table 6 at page 25 of the originally-filed specification and the disclosure in the Figures. To this end, the Examiner is courteously requested to review Example 11B at page 39 of the Training Materials. Although the subject matter discussed therein pertains to nucleic acid molecules, it is respectfully submitted that in view of the decision rendered on claim 2 of Example 11B, the entirety of Applicants' claims conforms with the PTO's published guidelines.

Thus it is respectfully submitted that the foregoing amendments render moot the written description rejection. The polypeptides are now claimed in terms of specific sequences. This is not to imply that the original claim scope was problematic under US law.

The contention that "Applicant has disclosed only the polypeptides of SEQ ID NO: 2, 4, [or] 6 encoded by SEQ ID NO: 1, 3 or 5" is incorrect. Applicants' specification provides a detailed disclosure of variant polypeptide molecules comprising one or more amino acid substitutions in the primary sequence of SEQ ID NO: 2. A total of eleven additional sequences (clones 1-11) are thus explicitly taught in these Examples. For example, clone 3 comprising P141, K282, L287, P299, L347, E351 variation in the polypeptide sequence of SEQ ID NO: 2, constitutes a variant polypeptide sequence whose structural information is expressly disclosed.

The structural information of other sequences can be similarly obtained. See, the paragraphs bridging page 24 and 25 of the present specification and the information provided in the sequence disclosure.

Sequence identity

A skilled artisan is thus in possession of the written description of both the nature (i.e., mutant or wild-type) as well as the structure (i.e., amino acid sequence) of the clone species disclosed in Table 6. Based on the information provided therein with respect to the polypeptide sequences, the skilled worker can ascertain the degree of sequence identity between the parent polypeptide of SEQ ID NO: 2 and the variant sequences (i.e., sequences comprising the recited amino acid variations in clones 1-11). Such techniques, comprising for example, computer assisted (i.e., BEST FIT) analysis or experimental analysis (i.e., hybridizationunder stringent conditions to a given polynucleotide and/or immunological cross-reactivity of the encoded polypeptide) were known in the art as of the filing date of the present application. Applicants' own specification provides a disclosure of such techniques. See, page 11, ¶3. Therefore it is respectfully submitted that the recited percent identity to a given sequence, for example, SEQ ID NO: 2, can thus be "at once envisaged." Explicit disclosure is not necessary. See, *Capon v. Eshhar v. Dudas,* (Fed. Cir. 2005) 418 F.3d 1349, 76 U.S.P.Q.2d 1078 (discussed *infra).*

Submitted herewith are exhibits disclosing the calculated sequence identities between the polypeptide molecules of the instant invention (in matrix form). In Exhibit A, full-length polypeptide sequences (for example, SEQ ID NO: 2, 4, 6 and the polypeptide sequences of the 11 different clones) have been compared. In Exhibits B and C, specific polypeptide fragments (of 144 amino acid residues and 33

amino acid residues, respectively) have been compared, it can be ascertained, for example, that the polypeptide of clone 3 comprising P 141, K282, L287, P299, L347, E351 variation in the polypeptide sequence ofSEQ ID NO: 2 has 98.8% sequence identity with that of SEQ ID NO: 2. The minimal structural identity between the claimed species of polypeptide molecules, for example, clone 1 and clone 9 (items 4 and 12 in the chart) is thus readily determined to be 90.8%. The structural features claimed herein, for example, sequence identity to a given polypeptide species, need not be explicitly disclosed in the instant application insofar as a generic teaching of such homologs and methods of determining the common structural features (i.e., sequence identity) have been provided. See, e.g., *In re Buchner,* 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, inc. v. MonoclonalAntibodies, Inc.,* 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). See, also, MPEP §2164.05(a).

Therefore claimed polypeptide molecules having the recited minimal sequence identity with the polypeptides of SEQ ID NO: 2 [see, sub-claim (c) of claim 13] or specific portion thereof [see, sub-claims (d) and (e) of claim 13] was taught by Applicants' own specification.

Enablement

Applicant respectfully traverses the PTO's contention that "the skilled artisan would not reasonably expect *anything less than 100% identity* over the full length of SEQ ID NO: 2, 4 or 6 to share the same function as the polypeptide of SEQ ID NO: 2, 4 or 6." In view of the aforementioned arguments and remarks, this contention is baseless.

Applicants' claims are directed to polypeptide molecules and fragments thereof comprising specific sequences. Variants of the claimed molecules, comprising, for example, the claimed sequence identity to a given polypeptide of SEQ ID NO:2, are further disclosed. The detailed disclosure contained in Applicants' specification (as substantiated by the disclosure of three polypeptide sequences and 1 t other clonal variants) provides a detailed description of the structure/activity of the claimed variant sequences. Structures (for example, amino acid sequences) of the claimed group 4 *Poaceae* allergens and clones thereof are provided in the sequence listing page mad the table at page 25. The biological activities of such polypeptide molecules, for example, with respect to their reactivity to IgE molecules, are also disclosed. See, the disclosure in Fig. 5 and the description thereof at page 6 of the present application.

Variant polypeptide sequences

Applicants invite the Examiner to review a recent precedential opinion issued by the United States Board of Patent Appeals and Interferences *(Ex parte* Kubin, B.A.P.I. 2007), a copy of which is enclosed herewith.

The facts in Kubin are applicable to the present case. In Kubin, the Examiner contended that *"at* least 80% identity language" in the absence of any working examples, other than a few representative species, fails to provide enablement of the claimed genus of molecules. See, page 10 *of Ex parte* Kubin. The Examiner alleged that specification did not teach "which 20%... of amino acid residues should be changed in order to maintain the biological functions." in response, Appellants argued that the specification disclosed *"in* detail how to: 1) make variants of SEQ ID NOs: 1 and 2; 2) calculate the percent identity between SEQ ID NOs: 1 and 2 and the variant sequence; and 3) test the variant sequence to determine [functional activity]." See, items 23 and 24 at page t 3. Appellants further argued that in view of the high level of skill in molecular biology, methods of making the claimed nucleic acid sequences and screening for activity [were] known in the art and described in the specification and that the "experimentation involved to produce other sequences within the scope of the claims" and thus to practice the full scope of the claims would have been "well within the skill of those in the art." The amount of experimentation involved would have been routine and not unduc. See, items 27-30 at page 14.

The Board of Patent Appeals and Interferences in reversing the enablement rejection concluded:

"The amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were welt known to those skilled in the art. *See, e.g., Johns Hopkins Univ. v. Cellpro, Inc.,* 152 F.3d 1342, 1360, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998)("test [for undue experimentation] is not merely quantitative.., if it is merely routine"). A "patent need not teach, and preferably omits, what is well known in the art." *Hybritech Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). Thus, we conclude the Specification would have enabled the full scope of claim 73.
(Emphasis added)

Likewise in the present application, Applicants disclose a genus of Phl p 4 (group 4 allergens) polypeptides having a disclosed primary structure and polynucleotides encoding such polypeptides. Methods of obtaining other polynucteotide sequences, for example, polynucleotides which hybridize to Phl p 4 polynucleotides of SEQ ID NO: 1, 3 and 5 under stringent hybridization conditions, were known in the art. Techniques for isolating polypeptide variants encoded by such hybridizing polynucleotides and methods for testing of such variant species based on claimed activity were all known in the art.

For example, a skilled artisan could routinely utilize translation techniques for identifying polypeptides which are encoded by such hybridizing polynucleotides (for example, using translation tools) and whether such polypeptides would meet the structural aspect(s) recited in Applicants' claims. The exhibits enclosed herewith provide an example via which variant sequences of Table 6 and/or fragments thereof may be analyzed with respect to the sequence identity to a given polypeptide sequence of SEQ ID NO: 2. Polypeptide sequences which meet the recited structural aspect(s) (for example, at least 90.8% sequence identity) could then be expressed and assayed for claimed igE activity using art-known techniques, for example, immunoblotting techniques. See, for example, the disclosure contained in Fig. 5. It would be routine that such polypeptides could be isolated and used by one of ordinary skill in the art using the methods recited in the instant application. Therefore, the level of "experimentation involved to produce other sequences within the scope of the claims" and thus to practice the full scope of the claims would have been "well within the skill of those in the art."

With respect to testing of the variant sequences, reference is made to several art publications which exemplify the various methods and high level of skill in the art that existed at the time the present application was filed for identifying such molecules. These references provide ample evidence that routine protocols for epitope mapping were available and being employed in a variety of fields prior to mad at the time of the filing of the present application. For example, Livingstone et al. *(Ann. Rev. Immunol.,* vol. 5,477-501, 1987) describe routine methods for identifying T cell epitope and provide models for predicting T cell epitopes in a protein on the basis of the primary sequence alone.

Moreover, synthesis of large arrays of unique peptides and use of such libraries for screening variants was routine in the art. For example, Geysen *(PNAS,* 81, 3998-4002. 1984) describes a method, subsequently referred to as "the pin method" or "the Pepscan method", which allows for the rapid, concurrent synthesis on polyethylene rods of hundreds of peptides of sufficient purify for ELISA assays. The screened peptides were mapped to epitopes of foot-and mouth disease virus coat protein involved in antibody binding. Subsequent publications by the same author expressly account for the routineness of the procedure. "The current methodology requires only basic skills in organic chemistry, and can be used to synthesize more than 2000 peptides (hexapeptides) per 10 working day." Geysen et al. further state their group "presently tests about 4000 peptides each working day." See, Geysen et al.,,l. *Immunol. Methods,* 259-274, 1987. Van der Zee et al. *(Eur. J. Immunol.* 1989.19:43-47) modified the Pepscan method so that the synthetic peptides could be released from the solid phase support, for direct use in T cell stimulation assays. Van der Zee used this modified technique to finely map a T-cell epitope in the mycobacteriai 65 kDa heat shock protein. Likewise, Maeji et al. used the Pepscan methodology to map T ceil epitopes of tetanus toxin (Maeji, et al., Multi-pin peptide synthesis strategy for T ceil determinant analysis. Jr. *of Immunol. Methods,* 134, 23-33. 1990). Since 1993, the Pepscan technique has been made commercially available in kit form by Cambridge Research Biochemicals, Cambridge, UK. For example, Cason used the Pepscan kit to map immunodominant epitope of the bovine papiltomavirus maj or (L I) capsid protein.

(Cason et al., *3. Gen. Virol.,* 74, 2669-2677, 1993). Likewise, Ebner et al. utilized the Pepscan method to identify multiple T cell epitopes on the major birch pollen allergen Bet vI. J. *of Immunol.,* 150, No.3, 1047-1054. 1993).

In addition to the Pepscan method, Houghten taught a method for synthesizing large numbers of peptides on standard, amino acid resin that was sealed in packets (the "teabag" method). See, Houghten et al., *PNAS,* 82, 5131-5135, 1985. Using this method, the synthetic peptides could be easily cleaved from the resin allowing them to be used in liquid phase assays. Houghten used this method to simultaneously synthesize 248 different peptides from the influenza hemagglutinin protein (HA 1), which were then used to map amino acids involved in the binding of anti-HA1 antibody. Houghten further states that his technique is simple and can be used to perform greater than 1000 syntheses simultaneously. Oftung et al. utilized the method of Houghten to map human T cell epitopes on the Mycobacterium tuberculosis 65-KD protein antigen *(J Imrnunol.,* 141, 2749-54, 1988). As an alternative to protein synthesis, the generation of peptides from a known protein sequence could have been achieved by genetic manipulation of nucleic acid molecules encoding the protein of interest. Relevant techniques include, for example, the use of frequently and non-frequently cutting, restriction enzymes to generate fragments of a nucleic acid molecule encoding the protein of interest; the use of timed exonuclease III and/or Dnase I digestions of a nucleic acid molecule encoding the protein of interest; and the use of the polymerase chain reaction to generate precise fragments of the open reading frame encoding the protein of interest. All of these techniques were being employed at the time of filing. The methodology for performing the aforementioned techniques is further provided in rich detail in Methods in Molecular Biology, vol. 66, Epitope Mapping Protocols, 1996.

Not only was it possible to easily generate a multitude of peptides from a known protein, but techniques for high-volume screening of such fragments and peptides for T cell epitopes were clearly available. For instance, such screening could have been achieved by measuring T-cell proliferation in response to peptides in combination with antigen presenting cells. Many of the references already mentioned describe such assays. For example, the aforementioned Van der Zee, Ebner, Oftung, and Lamb references, all teach assays using 3H-thymidine uptake by T cells as a way of measuring cell proliferation. Methods for assaying large number of samples, for example, employing a 96-well micro-plate, are also provided. It should be having a higher density of wells (e.g., 384 wells) along with the use of automated readers capable of handling such platforms were available to the skilled worker as of the filing date of the instant application. In addition, several methodologies were being used to increase the efficiency of such screening and/or isolation of peptides of interest.

Accordingly, it is respectfully submitted that at the time the present application was filed, routine methods were available to screen for specific epitopes and to test the effects contributed by the addition of each amino acid residue to a given epitope. For example, Focke et al. 2001 (cited in the Office Action) disclose Phi p 1 IgE epitopes and the functional background of generating peptides with reduced IgE reactivity (for example the destruction or deletion of IgE epitopes). Also Schramm et al. 1999 (see specification on page 3, first paragraph) disclose mutated recombinant allergens in which IgE epitopes are specifically deleted without impairing the T cell epitopes, which are essential for therapy.

Claims directed to the pharmaceutical composition/vaccines

In the paragraphs bridging pages 11 and 12, the Office Action alleges that the pharmaceutical compositions and/or vaccines of the present invention are non-enabled. This contention is respectfully traversed.

At the outset, Applicants courteously submit that the Office Action fails to present any evidence which suggests the pharmaceutical compositions, as claimed herein, are not enabled. In the absence of such evidence, the rejection is deficient under controlling case law.

The burden is upon the Patent and Trademark Office to provide evidence shedding doubt that the invention can not be made and used as stated; see for example, In re Marzocchi, 439, F. 2d 220, 169 USPQ

367 (CCPA 1971). Moreover, Applicants' specification teaches that molecules of the present invention are useful formulation of vaccines and/or pharmaceutical compositions. See the generic teachings offered in the paragraph bridging page 15 and 16 of the present application.

In relation to a disclosure on the utilization of Phl p 4 polypeptides as a pharmaceutical composition, the Examiner is courteously invited to review the disclosure contained in the Examples of the present application. See, for example, the paragraphs bridging page 7, line 28 to page 8, line 24 of the instant specification, as originally filed. In this regard, Applicants' specification expressly teaches that fragment and/or recombinant forms of allergens, which exhibit a different IgE reactivity profile compared to the natural allergen (nPhl p 4), can be noted that plates utilized as pharmaceutical compositions or vaccines. Rationale for the use of the molecules of the instant invention in the desensitization of a subject suffering from allergy is also provided. See, the page 15, lines 9-27; page 16, lines 19-24 of the specification, as originally filed.

Moreover, the disclosure in page 8, lines 3-17 of Applicants' specification and the cited Schramm reference expressly teach that the use of hypoallergenic peptide molecules, such as the rPht p 4 variant polypeptide of the present invention, for therapy of allergic diseases was appreciated by one of ordinary skilled in the art. To this end, the Examiner is also cordially requested to review the entirety of disclosure contained in the cited reference of Fischer et al. *(Journal of Allergy and Clinical Immunology,* 1996).

Thus it is respectfully submitted that the specification provides an enabling disclosure on the claimed allergenic properties of the Phl p 4 polypeptides of the instant invention. Therefore, the specification's express teaching that the claimed compounds are pharmaceutically useful is clearly credible as required. The PTO's contentions regarding non-enablement based on the "unpredictability" and "lack of working examples" are especially weak in view of the detailed disclosure contained in Applicants' own specification and the state of the art before the earliest filing date of the instant application. Withdrawal of the rejection is respectfully requested."

It is the Examiner's position that the Phl p 4 allergens disclosed in the specification cause disease (allergy) by definition. Therefore, the Examiner has met their burden in questioning whether or not Applicant's invention could be used as a pharmaceutical composition and/or vaccine with the ability to prevent allergy. Allergens, including Phl p 4, cause allergy and can lead to anaphylactic shock and death. Therefore, whether the claimed compositions will work in vivo is unpredictable, contrary to Applicant's assertion. Further, and as discussed *supra,* Applicant has not provided any evidence in the specification or otherwise to support their contention that the Phl p 4 allergens disclosed can be used in a vaccine to 100% prevent allergy, nor have they shown data that supports being able to generate antigen-specific antibody

responses and stimulation of memory T lymphocytes to protect or prevent against allergy.

As discussed supra, the specification fails to establish a correlation between the structure of the allergen necessary for the claimed functions for two reasons. First, the claimed functions "immunotherapeutic" "generating an immunomodulatoy, T-cell response in a host" and "T-cell reactive" are not specific enough functions that limit the claimed peptides to those with a testable function. The claimed functions are non-specific and therefore will not guide a skilled artisan to be able to make the correct polypeptides and peptides that can be used for the disclosed diagnostic and therapeutic purposes. In addition, the specification fails to disclose the regions of the phl p 4 allergen that are essential to giving the allergen its function. Therefore, one of ordinary skill in the art would not know which regions can be modified and which regions must be avoided when making variants that can be used for the diagnostic and therapeutic purposes disclosed in the specification. Therefore, the lack of specific guidance as to how structure of the molecule related to function of the molecule and the lack of requisite and sufficiently limited function in the claims, make the claims as recited not enabled.

12. Claims 13, 15 and 20-23 stand rejected and claims 25-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : polypeptides of SEQ ID NO: 2, 4, 6 encoded by SEQ ID NO:1, 3 or 5, respectively, the variants of SEQ ID NO:2 in clones 1-11 and a composition thereof.

Applicant is not in possession of : A polypeptide which is (a) a polypeptide which comprises the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6, (b) a polypeptide comprising a polypeptide sequence which is encoded by a the polynucleotide sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5, or (c) **a variant polypeptide which comprises at least 90.8% sequence identity** to the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 (d) **a polypeptide which comprises at least 79.9% sequence identity to the polypeptide comprising amino acids 219 to 362** of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6, (e) **a polypeptide which comprises at least 69.7% sequence identity to the polypeptide comprising amino acids 219 to 251** of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 of claim 13; A **pharmaceutical composition** comprising at least one polypeptide according to Claim 13 and a pharmaceutically acceptable carrier of claim 15; an immunotherapeutic vaccine comprising a polypeptide of claim 13 and an acceptable carrier, wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host of claim 20; an immunomodulatory, T-cell-reactive polypeptide fragment **which comprises a partial sequence of 50 to 350 amino acids of at least one polypeptide of claim 13** of claim 21; an immunomodulatory, T-cell-reactive **polypeptide fragment which comprises (a) fragment 1-200, with amino acids 1-200 of the polypeptide of claim 13**, or (b) **fragment 185-500, with amino acids 185-500 of the polypeptide of claim 13** of claim 22; **the variant**

polypeptide according to Claim 13 (c) which comprises a mutation, wherein said mutation results in the replacement of at least one cysteine residue of a polypeptide whose sequence is set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6 with another amino acid residue of claim 23; an immunotherapeutic vaccine comprising a **polypeptide of claim 13** and an acceptable carrier, wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host of claim 25; **A polypeptide according to claim 13** wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cell reactive response in a host of claim 26; an immunotherapeutic vaccine comprising **a polypeptide of claim 21** and an acceptable carrier, wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host of claim 27; an immunotherapeutic vaccine comprising **a polypeptide of claim 22** and an acceptable carrier, wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host of claim 28; An immunotherapeutic vaccine comprising **a polypeptide of claim 23** and an acceptable carrier, wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host of claim 29; A pharmaceutical composition comprising **at least one polypeptide according to claim 21** and a pharmaceutically acceptable carrier of claim 30; A pharmaceutical composition comprising **at least one polypeptide according to claim 22** and a pharmaceutically acceptable carrier of claim 31; A pharmaceutical composition comprising at **least one polypeptide according to claim 23** and a pharmaceutically acceptable carrier of claim 32; A polypeptide which comprises **(a) a polypeptide which is encoded by single nucleotide polymorph of a polynucleotide whose sequence is set forth in SEQ ID NO: 1, (b) a single amino acid polymorph of a polypeptide whose sequence is set forth in SEQ ID NO: 2** of claim 33; A

polypeptide which comprises **a polypeptide variant of the sequence set forth in SEQ ID NO: 2 with the amino acid variations set forth clones 1 to 11**:

(a) clone 1: L54, I57, V62, S76, T100, N107, Y137, P141, T142, K189, Q219, K221, L227, I231, **5235**, T237, V238, K248, A258, I264, K270, K282, L287, P299, A321, L322, S332, Q346, P347, T351, L357, N358, V362, S384, A410, D419, Y456, A457, K460, E472;

(b) clone 2: L54, I57, V62, T76, T100, N107, Y137, P141, T142, K189, Q219, K221, I231, S235, T237, V238, K248, A258, **1264**, K270, K282, L287, P299, A321, L322, S332, Q346, P347, T351, L357, N358, V362, **5384**, A410, D419, Y456, A457, K460, E472;

(c) clone 3: P141, K282, L287, P299, L347, E351;

(d) clone 4: G289, A410, D419, Y456, A457, K460, E472;

(e) clone 5: L347, E351, S384, A410, D419, Y456, A457, K460, E472;

(f) clone 6: NI07, Y137, P141, T142, K189, Q219, K221, I231, S235, T237, V238, K248, A258, I264, K270, K282, L287, P299, A321, L322, 5332, Q346, P347, T351, L357, N358, V362, S384, A410, D419, Y456, A457, K460;

(g) clone 7: K248, A258, I264, K270, K282, L287, P299, A321, L322, S332, Q346, P347,

T351, L357, N358, V362, S384;

(h) clone 8: Q219, K221, I231, S235, T237, V238, K248, A258, I264, K270, K282, L287,

P299, E351;

(i) clone 9: M231, T246, A251, C263, G289, L307, L309, E334;

(j) clone 10: Q219, K221, I231, S235, T237, M238, V242, V246, K248, A258, I264, K270, K282, L287, P299, A321, L322, S332, Q346, P347, T351, N358, V362, S384, insertion of GA between positions 407 and 408, N452, Y456, A457, K460, E472;

(k) clone 11: insertion of GA between positions 407 and 408.

Applicant has disclosed only the polypeptides of SEQ ID NO: 2, 4, 6 encoded by SEQ ID NO:1, 3 or 5, respectively and a composition thereof; therefore, the skilled artisan cannot

envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant's arguments filed on 06/03/2008 have been fully considered, but are not found persuasive.

Applicant argues:

"..Applicants' specification discloses a vast number of polypeptide species which comprise the claimed activity. See, Table 6 at page 25 of the originally-filed specification and the disclosure in the Figures. To this end, the Examiner is courteously requested to review Example 11B at page 39 of the Training Materials. Although the subject matter discussed therein pertains to nucleic acid molecules, it is respectfully submitted that in view of the decision rendered on claim 2 of Example 11B, the entirety of Applicants' claims conforms with the PTO's published guidelines.

Thus it is respectfully submitted that the foregoing amendments render moot the written description rejection. The polypeptides are now claimed in terms of specific sequences. This is not to imply that the original claim scope was problematic under US law.

The contention that "Applicant has disclosed only the polypeptides of SEQ ID NO: 2, 4, [or] 6 encoded by SEQ ID NO: 1, 3 or 5" is incorrect. Applicants' specification provides a detailed disclosure of variant polypeptide molecules comprising one or more amino acid substitutions in the primary sequence of SEQ ID NO: 2. A total of eleven additional sequences (clones 1-11) are thus explicitly taught in these Examples. For example, clone 3 comprising P141, K282, L287, P299, L347, E351 variation in the polypeptide sequence of SEQ ID NO: 2, constitutes a variant polypeptide sequence whose structural information is expressly disclosed.

The structural information of other sequences can be similarly obtained. See, the paragraphs bridging page 24 and 25 of the present specification and the information provided in the sequence disclosure.

Sequence identity

A skilled artisan is thus in possession of the written description of both the nature (i.e., mutant or wild-type) as well as the structure (i.e., amino acid sequence) of the clone species disclosed in Table 6.

Based on the information provided therein with respect to the polypeptide sequences, the skilled worker can ascertain the degree of sequence identity between the parent polypeptide of SEQ ID NO: 2 and the variant sequences (i.e., sequences comprising the recited amino acid variations in clones 1-11). Such techniques, comprising for example, computer assisted (i.e., BEST FIT) analysis or experimental analysis (i.e., hybridizationunder stringent conditions to a given polynucleotide and/or immunological cross-reactivity of the encoded polypeptide) were known in the art as of the filing date of the present application. Applicants' own specification provides a disclosure of such techniques. See, page 11, ¶3. Therefore it is respectfully submitted that the recited percent identity to a given sequence, for example, SEQ ID NO: 2, can thus be "at once envisaged." Explicit disclosure is not necessary. See, *Capon v. Eshhar v. Dudas,* (Fed. Cir. 2005) 418 F.3d 1349, 76 U.S.P.Q.2d 1078 (discussed *infra).*

Submitted herewith are exhibits disclosing the calculated sequence identities between the polypeptide molecules of the instant invention (in matrix form). In Exhibit A, full-length polypeptide sequences (for example, SEQ ID NO: 2, 4, 6 and the polypeptide sequences of the 11 different clones) have been compared. In Exhibits B and C, specific polypeptide fragments (of 144 amino acid residues and 33 amino acid residues, respectively) have been compared, it can be ascertained, for example, that the polypeptide of clone 3 comprising P 141, K282, L287, P299, L347, E351 variation in the polypeptide sequence ofSEQ ID NO: 2 has 98.8% sequence identity with that of SEQ ID NO: 2. The minimal structural identity between the claimed species of polypeptide molecules, for example, clone 1 and clone 9 (items 4 and 12 in the chart) is thus readily determined to be 90.8%. The structural features claimed herein, for example, sequence identity to a given polypeptide species, need not be explicitly disclosed in the instant application insofar as a generic teaching of such homologs and methods of determining the common structural features (i.e., sequence identity) have been provided. See, e.g., *In re Buchner,* 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, inc. v. MonoclonalAntibodies, Inc.,* 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). See, also, MPEP §2164.05(a).

Therefore claimed polypeptide molecules having the recited minimal sequence identity with the polypeptides of SEQ ID NO: 2 [see, sub-claim (c) of claim 13] or specific portion thereof [see, sub-claims (d) and (e) of claim 13] was taught by Applicants' own specification.

Enablement

Applicant respectfully traverses the PTO's contention that "the skilled artisan would not reasonably expect *anything less than 100% identity* over the full length of SEQ ID NO: 2, 4 or 6 to share the same function as the polypeptide of SEQ ID NO: 2, 4 or 6." In view of the aforementioned arguments and remarks, this contention is baseless.

Applicants' claims are directed to polypeptide molecules and fragments thereof comprising specific sequences. Variants of the claimed molecules, comprising, for example, the claimed sequence identity to a given polypeptide of SEQ ID NO:2, are further disclosed. The detailed disclosure contained in Applicants' specification (as substantiated by the disclosure of three polypeptide sequences and 11 other clonal variants) provides a detailed description of the structure/activity of the claimed variant sequences. Structures (for example, amino acid sequences) of the claimed group 4 *Poaceae* allergens and clones thereof are provided in the sequence listing page mad the table at page 25. The biological activities of such polypeptide molecules, for example, with respect to their reactivity to IgE molecules, are also disclosed. See, the disclosure in Fig. 5 and the description thereof at page 6 of the present application.

Variant polypeptide sequences

Applicants invite the Examiner to review a recent precedential opinion issued by the United States Board of Patent Appeals and Interferences *(Ex parte* Kubin, B.A.P.I. 2007), a copy of which is enclosed herewith.

The facts in Kubin are applicable to the present case. In Kubin, the Examiner contended that *"at* least 80% identity language" in the absence of any working examples, other than a few representative species, fails to provide enablement of the claimed genus of molecules. See, page 10 *of Ex parte* Kubin. The Examiner alleged that specification did not teach "which 20%... of amino acid residues should be changed in order to maintain the biological functions." in response, Appellants argued that the specification disclosed *"in* detail how to: 1) make variants of SEQ ID NOs: 1 and 2; 2) calculate the percent identity between SEQ ID NOs: 1 and 2 and the variant sequence; and 3) test the variant sequence to determine [functional activity]." See, items 23 and 24 at page t 3. Appellants further argued that in view of the high level of skill in molecular biology, methods of making the claimed nucleic acid sequences and screening for activity [were] known in the art and described in the specification and that the "experimentation involved to produce other sequences within the scope of the claims" and thus to practice the full scope of the claims would have been "well within the skill of those in the art." The amount of experimentation involved would have been routine and not undue. See, items 27-30 at page 14.

The Board of Patent Appeals and Interferences in reversing the enablement rejection concluded:

"The amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were welt known to those skilled in the art. *See, e.g., Johns Hopkins Univ. v. Cellpro, Inc.,* 152 F.3d 1342, 1360, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998)("test [for undue experimentation] is not merely quantitative.., if it is merely routine"). A "patent need not teach, and preferably omits, what is well known in the art." *Hybritech Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). Thus, we conclude the Specification would have enabled the full scope of claim 73.
(Emphasis added)

Likewise in the present application, Applicants disclose a genus of Phl p 4 (group 4 allergens) polypeptides having a disclosed primary structure and polynucleotides encoding such polypeptides. Methods of obtaining other polynucteotide sequences, for example, polynucleotides which hybridize to Phl p 4 polynucleotides of SEQ ID NO: 1, 3 and 5 under stringent hybridization conditions, were known in the art. Techniques for isolating polypeptide variants encoded by such hybridizing polynucleotides and methods for testing of such variant species based on claimed activity were all known in the art.

For example, a skilled artisan could routinely utilize translation techniques for identifying polypeptides which are encoded by such hybridizing polynucleotides (for example, using translation tools) and whether such polypeptides would meet the structural aspect(s) recited in Applicants' claims. The exhibits enclosed herewith provide an example via which variant sequences of Table 6 and/or fragments thereof may be analyzed with respect to the sequence identity to a given polypeptide sequence of SEQ ID NO: 2. Polypeptide sequences which meet the recited structural aspect(s) (for example, at least 90.8% sequence identity) could then be expressed and assayed for claimed igE activity using art-known techniques, for example, immunoblotting techniques. See, for example, the disclosure contained in Fig. 5. It would be routine that such polypeptides could be isolated and used by one of ordinary skill in the art using the methods recited in the instant application. Therefore, the level of "experimentation involved to produce other sequences within the scope of the claims" and thus to practice the full scope of the claims would have been "well within the skill of those in the art."

With respect to testing of the variant sequences, reference is made to several art publications which exemplify the various methods and high level of skill in the art that existed at the time the present application was filed for identifying such molecules. These references provide ample evidence that routine protocols for epitope mapping were available and being employed in a variety of fields prior to mad at the time of the filing of the present application. For example, Livingstone et al. *(Ann. Rev. Immunol.,* vol. 5,477-501, 1987) describe routine methods for identifying T cell epitope and provide models for predicting T cell epitopes in a protein on the basis of the primary sequence alone.

Moreover, synthesis of large arrays of unique peptides and use of such libraries for screening variants was routine in the art. For example, Geysen *(PNAS,* 81, 3998-4002. 1984) describes a method, subsequently referred to as "the pin method" or "the Pepscan method", which allows for the rapid, concurrent synthesis on polyethylene rods of hundreds of peptides of sufficient purify for ELISA assays. The screened peptides were mapped to epitopes of foot-and mouth disease virus coat protein involved in antibody binding. Subsequent publications by the same author expressly account for the routineness of the procedure. "The current methodology requires only basic skills in organic chemistry, and can be used to synthesize more than 2000 peptides (hexapeptides) per 10 working day." Geysen et al. further state their group "presently tests about 4000 peptides each working day." See, Geysen et al.,,l. *Immunol. Methods,* 259-274, 1987. Van der Zee et al. *(Eur. J. Immunol.* 1989.19:43-47) modified the Pepscan method so that the synthetic peptides could be released from the solid phase support, for direct use in T cell stimulation assays. Van der Zee used this modified technique to finely map a T-cell epitope in the mycobacteriai 65 kDa heat shock protein. Likewise, Maeji et al. used the Pepscan methodology to map T ceil epitopes of tetanus toxin (Maeji, et al., Multi-pin peptide synthesis strategy for T ceil determinant analysis. Jr. *of Immunol. Methods,* 134, 23-33. 1990). Since 1993, the Pepscan technique has been made commercially available in kit form by Cambridge Research Biochemicals, Cambridge, UK. For example, Cason used the Pepscan kit to map immunodominant epitope of the bovine papiltomavirus maj or (L I) capsid protein. (Cason et al., *3. Gen. Virol.,* 74, 2669-2677, 1993). Likewise, Ebner et al. utilized the Pepscan method to identify multiple T cell epitopes on the major birch pollen allergen Bet vI. J. *of Immunol.,* 150, No.3, 1047-1054. 1993).

In addition to the Pepscsan method, Houghten taught a method for synthesizing large numbers of peptides on standard, amino acid resin that was sealed in packets (the "teabag" method). See, Houghten et al., *PNAS,* 82, 5131-5135, 1985. Using this method, the synthetic peptides could be easily cleaved from the resin allowing them to be used in liquid phase assays. Houghten used this method to simultaneously synthesize 248 different peptides from the influenza hemagglutinin protein (HA 1), which were then used to map amino acids involved in the binding of anti-HA1 antibody. Houghten further states that his technique is simple and can be used to perform greater than 1000 syntheses simultaneously. Ofiung et al. utilized the method of Houghten to map human T cell epitopes on the Mycobacterium tuberculosis 65-KD protein antigen *(J Imrnunol.,* 141, 2749-54, 1988). As an alternative to protein synthesis, the generation of peptides from a known protein sequence could have been achieved by genetic manipulation of nucleic acid molecules encoding the protein of interest. Relevant techniques include, for example, the use of frequently and non-frequently cutting, restriction enzymes to generate fragments of a nucleic acid molecule encoding the protein of interest; the use of timed exonuclease III and/or Dnase I digestions of a nucleic acid molecule encoding the protein of interest; and the use of the polymerase chain reaction to generate precise fragments of the open reading frame encoding the protein of interest. All of these techniques were being employed at the time of filing. The methodology for performing the aforementioned techniques is further provided in rich detail in Methods in Molecular Biology, vol. 66, Epitope Mapping Protocols, 1996.

Not only was it possible to easily generate a multitude of peptides from a known protein, but techniques for high-volume screening of such fragments and peptides for T cell epitopes were clearly available. For instance, such screening could have been achieved by measuring T-cell proliferation in response to peptides in combination with antigen presenting cells. Many of the references already mentioned describe such assays. For example, the aforementioned Van der Zee, Ebner, Ofung, and Lamb references, all teach assays using 3H-thymidine uptake by T cells as a way of measuring cell proliferation. Methods for assaying large number of samples, for example, employing a 96-well micro-plate, are also provided. It should be having a higher density of wells (e.g., 384 wells) along with the use of automated readers capable of handling such platforms were available to the skilled worker as of the filing date of the instant application. In addition, several methodologies were being used to increase the efficiency of such screening and/or isolation of peptides of interest.

Accordingly, it is respectfully submitted that at the time the present application was filed, routine methods were available to screen for specific epitopes and to test the effects contributed by the addition of

> each amino acid residue to a given epitope. For example, Focke et al. 2001 (cited in the Office Action) disclose Phi p 1 IgE epitopes and the functional background of generating peptides with reduced IgE reactivity (for example the destruction or deletion of IgE epitopes). Also Schramm et al. 1999 (see specification on page 3, first paragraph) disclose mutated recombinant allergens in which IgE epitopes are specifically deleted without impairing the T cell epitopes, which are essential for therapy."

It is the Examiner's position that the specification does not disclose a correlation structure of the allergen and variants and function ("generating an immunomodulatory, T-cell response in a host" and "T -cell reactive") such that a skilled artisan would have known what modification to make to the Phl p 4 allergens to attain the claimed functions. "Possession may not be shown by merely describing how to obtain possession of member of the claimed genus or how to identify their common structural features" *Ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)), at page 16. In this instant case Applicants have not provided any guidance as to what variants will result in the claimed functions. "Without a correlation between structure and function, the claim does little more than define the claimed invention by function" *supra*, at page 17. Definition by function does not suffice to define the genus because it is only an indication of what the allergen does and what functional properties it has, rather than what it is.

13. Claims 13, 15, 20-23 and 25-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a New Matter rejection for the following reasons:

The phrases "a variant polypeptide which comprises at least 90.8% sequence identity to the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6" claimed in claim 13(c), "polypeptide which comprises at least 79.9% sequence identity to the polypeptide comprising amino acids 219 to 362 of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6" in claim 13(d); and "polypeptide which comprises at least 69.7% sequence identity to the polypeptide comprising amino acids 219 to 251 of the polypeptide sequence set forth in SEQ ID NO: 2" in claim 13(e), "a partial sequence of 50 to 350 amino acids of at least one polypeptide of claim 13" of claim 21, "fragment 1-200, with amino acids 1-200 of the polypeptide of claim 13" and "fragment 185-500, with amino acids 185-500 of the polypeptide of claim 13" of claim 22; and "the variant polypeptide according to Claim 13(c) which comprises a mutation wherein said mutation results in the replacement of at least one cysteine residues of a polypeptide whose sequence is set forth in SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO;6 with another amino acids residue.' of claim 23 introduced by the amendment filed 06/03/2008 represents a departure from the specification and the claims as originally filed.

Applicant's amendment points to "express disclosure contained in the Examples and the sequence listing page" in addition to Applicant's analysis listed in Exhibits A-C. Applicant claims that the minimal sequence identity as recited in sub-claims 13 (c)-(e) can be "at once invisaged" based on the teachings of the present application, particularly as disclosed in clone 1-11. However, the specification and the claims as originally filed do not provide a clear support for the phrases "a variant polypeptide which comprises at least 90.8% sequence identity to the

polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6" claimed in claim 13(c), "polypeptide which comprises at least 79.9% sequence identity to the polypeptide comprising amino acids 219 to 362 of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6" in claim 13(d); and "polypeptide which comprises at least 69.7% sequence identity to the polypeptide comprising amino acids 219 to 251 of the polypeptide sequence set forth in SEQ ID NO: 2" in claim 13(e), "a partial sequence of 50 to 350 amino acids of at least one polypeptide of claim 13" of claim 21, "fragment 1-200, with amino acids 1-200 of the polypeptide of claim 13" and "fragment 185-500, with amino acids 185-500 of the polypeptide of claim 13" of claim 22; and "the variant polypeptide according to Claim 13(c) which comprises a mutation wherein said mutation results in the replacement of at least one cysteine residues of a polypeptide whose sequence is set forth in SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO;6 with another amino acids residue.' of claim 23.

The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112. It is noted that, at best, calculations derived from clones 1-11 provide support for a polypeptide variant having the exact percentages of sequence identity to SEQ ID NO:2 represented by each clone and having the exact variations recited in each clone. However, they do not provide support for the genus of variant polypeptides which comprise at least 90.8%, 79.9% or 69.7% sequence identity or those variant polypeptides having additional

variations or fragments thereof.

Obviousness is not the standard for the addition new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). New Matter is a written description issue.

Applicant is required to cancel the New Matter in the response to this Office Action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 13, 15, 20-22 and 25-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Fischer et al. (PTO-892 mailed on 06/07/2007, Reference U).

Fischer et al teaches isolation of the allergen Phl p 4 from Phleum pratense in a pharmaceutically acceptable carrier (Tris-buffered saline or water) (In particular, 'Methods' section on pages 190-192, whole document).

The recitations of "which comprises the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6"; "which is encoded by a the polynucleotide sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5"; "variant polypeptide which comprises at least 90.8% sequence identity to the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6"; " a polypeptide which comprises at least 79.9% sequence identity to the polypeptide comprising amino acids 219 to 362 of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6"; and "a polypeptide which comprises at least 69.7% sequence identity to the polypeptide comprising amino acids 219 to 251 of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6" of claim 13; "comprises a partial sequence of 50 to 350 amino acids of at least one polypeptide of claim 13" of claim 21; "comprises (a) fragment 1-200, with amino acids 1-200 of the polypeptide of claim 13, or (b) fragment 185-500, with amino acids 185-500 of the polypeptide of claim 13" of claim 22; "comprises (a) a polypeptide which is encoded by single nucleotide polymorph of a polynucleotide whose sequence is set forth in SEQ ID NO: 1, (b) a single amino acid polymorph of a polypeptide whose sequence is set forth in SEQ ID NO: 2" of claim 33; and "comprises a

polypeptide variant of the sequence set forth in SEQ ID NO: 2" of claim 34. The reference Phl p 4 molecule is the same as the protein of claims. Further characterization of a known compound does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art."

The recitations of "wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host" of claims 20, 25 and 27-29; "immunomodulatory T cell reactive polypeptide fragment" of claims 21 and 22; and "wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cell reactive response in a host" of claim 26 are inherent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced Phl p 4 allergen. Products of identical chemical composition cannot have mutually exclusive properties because a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an

inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

It is noted in the specification on page 14 that there are three natural isoforms of the heterogenous Phl p 4 allergen molecule (SEQ ID NOs 2, 4 and 6). Since the office does not have a laboratory to test the reference Phl p 4 allergen, it is applicant's burden to show that the reference allergen does not comprise the amino acid sequences of SEQ ID NO:2, 4 and 6 recited in the claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant's arguments filed on 06/03/2008 have been fully considered, but are not found persuasive.

Applicant argues:

> "Fischer teaches decapeptide sequence of Phl p 4 containing ten amino acid residues (IVALPXGMLK) of the N-terminal region of Phl p 4. See, Fig. 5 and the description thereof at page 194 of Fischer et al. Fischer fails to teach or suggest the polypeptides of the present invention, for example, a polypeptides which comprise the sequences set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6, or fragments thereof, as recited in present claim 13. Moreover, the cited reference fails to teach or suggest the structural elements of the polypeptides, comprising, for example, 50-350 amino acid residues. See, amended claim 21. Since not all elements of Applicants' claims are taught by Fischer, the cited reference fails to anticipate what is claimed herein. Withdrawal of the rejection is respectfully requested."

It is the Examiner's position that the prior anticipates the amended claims for the reasons as set forth *supra*.

16. Claims 13, 15, 20-22 and 25-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Suck et al. (Reference 4; IDS filed 12/23/2004).

Suck et al teaches isolation of the allergen Phl p 4 from Phleum pratense in a pharmaceutically acceptable carrier (water) (In particular, 'Materials and Methods' section on page 1396, Figure 4, whole document).

The recitations of "which comprises the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6"; "which is encoded by a the polynucleotide sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5"; "variant polypeptide which comprises at least 90.8% sequence identity to the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6"; " a polypeptide which comprises at least 79.9% sequence identity to the polypeptide comprising amino acids 219 to 362 of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6"; and "a polypeptide which comprises at least 69.7% sequence identity to the polypeptide comprising amino acids 219 to 251 of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6" of claim 13; "comprises a partial sequence of 50 to 350 amino acids of at least one polypeptide of claim 13" of claim 21; "comprises (a) fragment 1-200, with amino acids 1-200 of the polypeptide of claim 13, or (b) fragment 185-500, with amino acids 185-500 of the polypeptide of claim 13" of claim 22; "comprises (a) a polypeptide which is encoded by single nucleotide polymorph of a polynucleotide whose sequence is set forth in SEQ ID NO: 1, (b) a single amino acid polymorph of a polypeptide whose sequence is set forth in SEQ ID NO: 2" of claim 33; and "comprises a polypeptide variant of the sequence set forth in SEQ ID NO: 2" of claim 34. The reference Phl p 4 molecule is the same as the protein of claims. Further characterization of a known compound

does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art."

The recitations of "wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host" of claims 20, 25 and 27-29; "immunomodulatory T cell reactive polypeptide fragment" of claims 21 and 22; and "wherein each of the polypeptides of (a) to (e) is immunogenic and induces an immunomodulatory T-cell reactive response in a host" of claim 26 are inherent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced Phl p 4 allergen. Products of identical chemical composition cannot have mutually exclusive properties because a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re

Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

It is noted in the specification on page 14 that there are three natural isoforms of the heterogenous Phl p 4 allergen molecule (SEQ ID NOs 2, 4 and 6). Since the office does not have a laboratory to test the reference Phl p 4 allergen, it is applicant's burden to show that the reference allergen does not comprise the amino acid sequences of SEQ ID NO:2, 4 and 6 recited in the claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

17. Claims 13, 15, 20-22 and 25-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Fahlbusch et al. (Reference 3; IDS filed on 12/23/2004).

Fahlbusch et al teaches isolation of the allergen Phl p 4 from Phleum pratense in a pharmaceutically acceptable carrier (water) (In particular, 'Methods' section; paragraph spanning pages 801-802, Figure 1; whole document).

The recitations of "which comprises the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6"; "which is encoded by a the polynucleotide sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5"; "variant polypeptide which comprises at least 90.8% sequence identity to the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6"; " a polypeptide which comprises at least 79.9% sequence identity to the polypeptide comprising amino acids 219 to 362 of the polypeptide sequence set

forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6"; and "a polypeptide which comprises at least 69.7% sequence identity to the polypeptide comprising amino acids 219 to 251 of the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6" of claim 13; "comprises a partial sequence of 50 to 350 amino acids of at least one polypeptide of claim 13" of claim 21; "comprises (a) fragment 1-200, with amino acids 1-200 of the polypeptide of claim 13, or (b) fragment 185-500, with amino acids 185-500 of the polypeptide of claim 13" of claim 22; "comprises (a) a polypeptide which is encoded by single nucleotide polymorph of a polynucleotide whose sequence is set forth in SEQ ID NO: 1, (b) a single amino acid polymorph of a polypeptide whose sequence is set forth in SEQ ID NO: 2" of claim 33; and "comprises a polypeptide variant of the sequence set forth in SEQ ID NO: 2" of claim 34. The reference Phl p 4 molecule is the same as the protein of claims. Further characterization of a known compound does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art."

The recitations of "wherein said vaccine is capable of generating an immunomodulatory, T-cell response in a host" of claims 20, 25 and 27-29; "immunomodulatory T cell reactive polypeptide fragment" of claims 21 and 22; and "wherein each of the polypeptides of (a) to (e) is

immunogenic and induces an immunomodulatory T-cell reactive response in a host" of claim 26 are inherent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced Phl p 4 allergen. Products of identical chemical composition cannot have mutually exclusive properties because a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

It is noted in the specification on page 14 that there are three natural isoforms of the heterogenous Phl p 4 allergen molecule (SEQ ID NOs 2, 4 and 6). Since the office does not have a laboratory to test the reference Phl p 4 allergen, it is applicant's burden to show that the reference allergen does not comprise the amino acid sequences of SEQ ID NO:2, 4 and 6 recited in the claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

18. No claim is allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 9, 2008
Nora M. Rooney, M.S., J.D.
Patent Examiner
Technology Center 1600

/Maher M. Haddad/
Maher M. Haddad, Ph.D.
Primary Examiner,
Art Unit 1644